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Role of gamma-glutamyl transferase in evolution of coronary artery disease

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KEYWORDS

Gamaglutamyl transferase;
Atherosclerosis;
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Lipid profile.

A B S T R A C T

Gammaglutamyltransferases is a serum transferase synthesized by liver. It is commonly used in clinical practice to monitor liver function, alcohol consumption and hepatobiliary disorders. It has been proposed that gamglutamyltransferase is a potent biochemical marker for preclinical development of atherosclerosis. To evaluate the association of serum Gammaglutamyltransferase activity with lipid profile in coronary artery disease. This cross sectional study comprised 100 subjects, which included equal number of healthy volunteers and myocardial infarction cases. Serum Gammaglutamyl transferase activity and lipid profile was estimated. The data was statistically analyzed. The serum Gammaglutamyltransferase activity, cholesterol, triglycerides and low density lipoprotein were increased in myocardial infarction patients. Serum Gammaglutamyl transferase correlated with the lipid parameters in myocardial infraction patients. GGT can be used a potent biochemical marker for preclinical development of atherosclerosis.

Introduction

Gamma Glutamyl Transferase (E.C 2.3.2.1, GGT) is an enzyme present in serum and cell surface (Tatjana Stojakovic et al., 2009). It is a dimeric protein found attached to cell membrane, serum albumin and lipoproteins(Hidenari et al., 2005). It is present in kidney, lymphocytes, lungs, brain etc with predominance in liver (Mehmet Yunus et al., 2010). It is commonly used in clinical practice to monitor liver function, alcohol consumption and hepatobiliary disorders (Whitfield, 2001). It is known functions are transfer of amino acids across cell membrane and glutathione metabolism (Duk-Hee Lee et al., 2004). Its role in

oxidative stress, inflammation and endothelial dysfunction have been discovered (Sharma et al., 2010). Recently it has been proposed that GGT is a potent biochemical marker for preclinical development of atherosclerosis (Okan Turgut et al., 2009; Aldo paolicchi et al., 2005). It may affect lipid metabolism leading to hypercholesterolaemia and hypertriglyceridemia (Douglas et al., 2007; Tatjana Shipilova et al., 2006).

Laboratory diagnostics of disturbances in lipid metabolism employ a wide range of biochemical indicators (Nwagha et al., 2010). Lipid profile consists of a group of biochemical tests often used for predicting, diagnosing and treating lipid related disorders including atherosclerosis (Tariq M AQli Rajab). It usually consists of total cholesterol, triglyceride, low density lipoprotein and high density lipoprotein estimation (Yadav Arvind and Bhagwant Vinod, 2012).

Adverse lipid profile have been recognized as independent risk factor for coronary artery disease (Adak and Shivapuri, 2012). The atherogenic lipid profile is characterized by increased total cholesterol, triglyceride, low density lipoprotein and decreased high density lipoprotein. Abnormalities in lipid profile are major risk factors for coronary artery disease (Limba et al., 2008).

We hypothesize that serum Gamma Glutamyl Transferase activity may play a significant role in lipid metabolism leading to intiation and progression of coronary artery disease. The study was done to evaluate the relation between serum gamglutamyl transferase activity with serum lipids and lipoproteins.

The objectives of this study are:

To compare the Gamma Glutamyl Transferase activity and lipid profile in healthy volunteers and myocardial infarction patients.

To correlate serum Gamma Glutamyl Transferase activity with lipid profile in healthy volunteers and myocardial infarction patients.

Materials and Methods

The research protocol was approved by M.R.Medical College's Ethical Committee. This analytical observational cross sectional study was carried out at Basaveshwar Teaching & General Hospital, Gulbarga, Karnataka for a period of one year from 01.11.2010 to 31.10.2011.

The study subjects were selected by simple random sampling. They comprised of 100 subjects divided into 2 equal groups – cases and controls. The cases group included myocardial infarction patients and healthy volunteers were included in control group. The study subjects were selected by the following inclusion and exclusion criteria. The patients between 30 to 60 years of age ,both sex and myocardial infarction were included for the study. Patients with history of cardiac risk factors ,any systemic illness, recent surgery or trauma, endocrinal and nutritional disorders, pregnant women, drugs affecting lipid metabolism and alcholism were excluded.

The equipment used for the study are BD vacutainers, syringes, Biohit Micropippettes, Remi Centrifuge and Erba Chem 7 Semi-auto analyzer. The reagent kits for biochemical estimations were obtained from Agappe Diagnostics. The material used for this study consists of well

structured questionnaire and blood samples. Before participation, the volunteers were explained about the nature and purpose of the study. A voluntarily signed written consent was obtained from them.

A detailed history was obtained by the cardiologist and a complete physical examination was done with special emphasis on cardiovascular disease. Diagnosis of myocardial infarction was done based on ECG changes or rise in cardiac biomarkers. 2 ml of overnight fasting blood sample was collected aseptically from median cubital vein of each individual with a disposable plastic syringe with needle gauge No. 20 into a plain vacutainer. Blood was allowed to clot and then centrifuged at 4000 RPM for 15 minutes to obtain serum. The serum sample was subjected to the following biochemical estimations,

Gamma Glutamyl Transferase activity by SZASZ method,
CKMB activity by immunological UV-assay,
Troponin I by immunochromatography card method,
Total cholesterol by CHOD-PAP method,
Triglycerides by GPO PAP ESPAS method,
HDL by turbidometric immunoassay,
LDL by enzyme selective precipitation method.

The reference ranges of above parameters were

CKMB- 0-24 IU/L
GammaGlutamylTransferase-10 – 40 IU/L
Total cholesterol - 150-200 mg/dL
Triglycerides - 50-150 mg/dL
HDL 35-70 mg/dL
LDL - 80-130 mg/dL

The descriptive analysis of the data was done by mean and standard deviation. The comparison of parameters between cases and controls were done by unpaired 2-tailed t-test. $p<0.05$ was considered statistically significant. The association between Gamma Glutamyl Transferase and lipid variables was analyzed by Pearson correlation coefficient test. Statistical analysis of the data by using statistical data analysis software SPSS Version-1.7.

Result and Discussion

The data from the above analysis were compiled into two tables i.e., Table-1 and Table-2.

Table-1 compares the mean value of the variables in healthy volunteers and myocardial infarction patients. The difference for age and sex were not statistically significant. Statistically significant differences were seen for Gammaglutamyltransferase activity, cholesterol, triglycerides and lipoproteins values.

Table-2 shows the association of serum Gammaglutamyltransferase activity with cholesterol , triglycerides, high density and low density lipoproteins. The enzyme activity showed statistically significant correlation with the atherogenic lipids.

The study was done to evaluate the relationship of serum Gammaglutamyltransferase activity with lipid profile in coronary heart disease.

Table.1 Comparison of GGT and lipid profile in controls & cases

Parameters (units)	Cases	Controls	' p' value	Significance
GGT(IU/L)	32±12.07	15±3	<0.001	VHS
Total Cholesterol(mg/dl)	166±28	154.±17	<0.05	S
Triglyceride(mg/dl)	1398±53	95± 9.61	<0.005	HS
HDL-Cholesterol (mg/dl)	40±8	45±9	<0.05	S
LDL- Cholesterol(mg/dl)	103±24	84±19	<0.05	S

VHS = very highly significant**,HS**= highly significant **, S**=significant **.**

Table.2 Correlation of GGT activity with lipid profile components in cases and controls

Lipid profile	Cases (r value)	Controls (r value)
Total Cholesterol (mg/dl)	0.57**	0.12
Triglyceride (mg/dl)	0.58**	0.04
HDL-Cholesterol (mg/dl)	-0.44*	-0.30
LDL- Cholesterol (mg/dl)	0.53	0.37

**Correlation is significant at the 0.01 level (2-tailed)
*Correlation is significant at the 0.05 level (2-tailed).

Fig.1 GGT Comparison in Controls and Cases

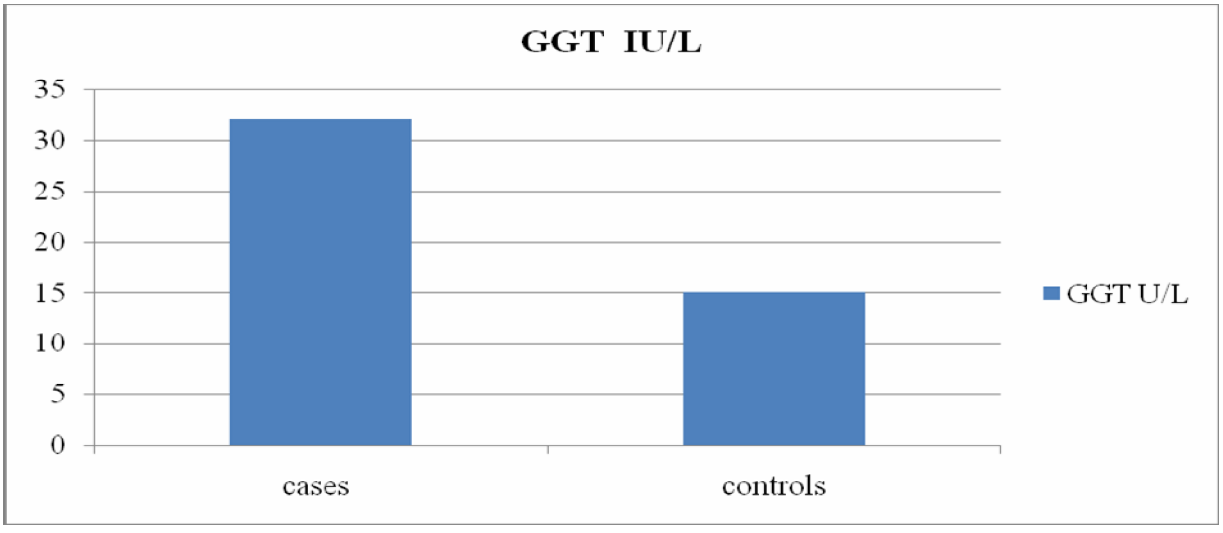


Fig.2 Correlation of GGT VS TC in myocardial infraction patients

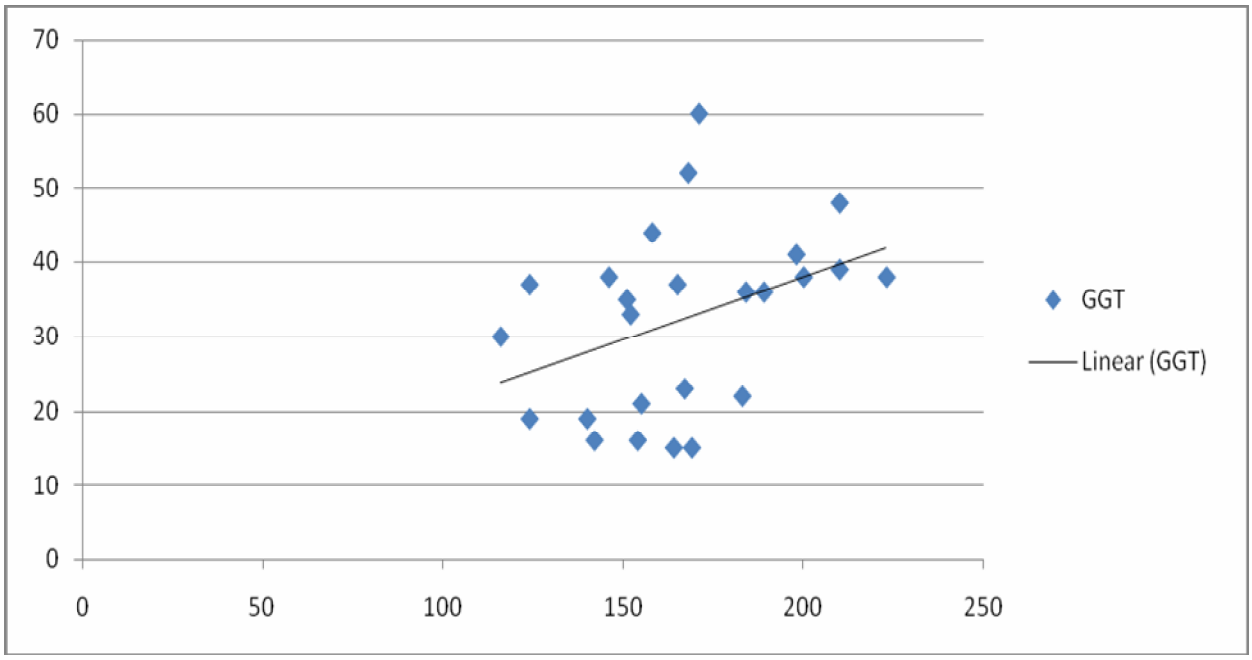
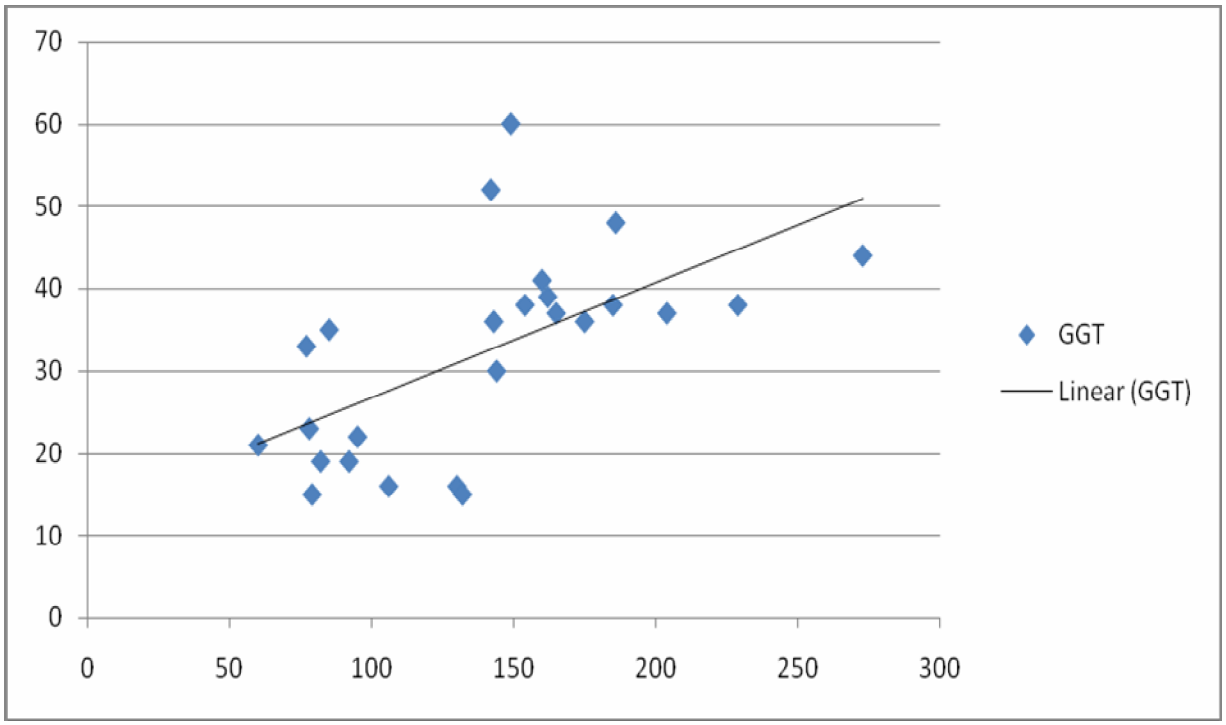


Fig.3 Correlation of GGT Vs TG in myocardial infraction patients



In the present study, we have compared the values of Gammaglutamyl transferase activity and lipid profile in healthy subjects and myocardial infarction patients. Also we correlated the Gammaglutamyl transferase activity with lipid profile. We found increase in Gammaglutamyl transferase, cholesterol, triglycerides in myocardial infarction patients. Gammaglutamyl transferase activity was associated with the lipid components. Increased Gammaglutamyl transferase oxidizes LDL to form oxidised LDL which is cleared slowly from circulation. Hence LDL levels are increased with corresponding increase total cholesterol of blood. Increase in triglycerides decreases HDL levels. Increased low density lipoproteins and triglycerides cause atherosclerosis (Alfonso Pompella, et al., 2004). The findings of our study were similar to other studies done (Emdin et al., 2001). To conclude gamaglutamyl transferase activity is associated with lipid profile. GGT may be used as a potent biochemical marker for preclinical development of atherosclerosis .Further in vitro research work can be carried out to elucidate the detailed mechanism by which gamaglutamyl transferase plays a significant role in atherosclerosis.

The strength of the work lies in standardized protocol, examination by experienced cardiologist and biochemist. The limitations of the study, where the cross sectional study design, small sample size, subjects not sex matched, single measurements. The demographic and clinical data are lacking. Enzymes and other metabolites of lipid metabolism not estimated.

No conflict of interest was declared. All authors contributed in designing of study, collection, analysis, interpretation of study and manuscript preparation. We would like to thank the Dean, Medical Superintendent, Cardiologist, Technicians, patients and volunteers for their cooperation in carrying out the study.

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